REMARKS

Claims 1-48 are pending in the above-identified application. Claims 7-46 have been cancelled without prejudice as being drawn to a non-elected invention. Applicant reserves the right to pursue these claims in a later filed application claim benefit of priority to the above-identified application. Accordingly, claims 1-6, 47 and 48 are currently under examination.

Claims 1-4, 47 and 48 have been indicated to be allowable in the Office Action mailed March 11, 2003. Claim 6 has been amended above. The amendment parallels Applicant's previous amendment to claim 1 reciting that the claimed human monoclonal antibody binds the same neoplastic cell or antigen as the antibody set forth in SEQ ID NOS:2 and 4. Support for the amendment can be in the specification at, for example, page 8, lines 1-16; page 15, line 9 through page 16, line 2; page 16, lines 10-21; page 21, lines 3-5; page 22, line 22 through page 23, line 7, and at page 28, lines 9-14. Accordingly, the amendment does not introduce new matter and entry thereof is respectfully requested.

Applicant thanks Examiner Helms for extending a personal interview with Applicant's representative on April 30, 2003. During the interview the rejections of claims 5 and 6 under 35 U.S.C. §112, first paragraph were discussed. The above amendment and the remarks set forth below are responsive to the rejections discussed during the interview.

Rejections Under 35 U.S.C. §112, First Paragraph

Claim 5 remains rejected under 35 U.S.C. §112, first paragraph, as lacking enablement allegedly because the data supporting enablement is based on in vitro cell culture whereas the claim, directed to a pharmaceutical composition, reads on in vivo treatment of cancer. Undue experimentation is allegedly required because the art does not recognize a clear correlation between in vivo and in vitro data and the claimed antigens have not clearly been demonstrated as a target for cancer therapy.

Applicant maintains that any use that reasonably correlates with the scope of the claim is sufficient to preclude a rejection for nonenablement based on how to use. To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *Genentech, Inc. v. Novo Nodisk A/S*, 108 F.3d 1361, 1365, 42 U.S.P.Q.2d 1001, 1004 (Fed. Cir. 1997), *see also* MPEP §2164.01(c), fourth paragraph. Further, in *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1360 (Fed. Cir. 1998), the Federal Circuit clearly stated that routine experimentation does not constitute undue experimentation:

> The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to

> enable the determination of how to practice a desired embodiment of the invention claimed.

Id. (*citing PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564 (Fed. Cir. 1996); *see also In re Wands*, 858 F.2d 731, 736-40 (Fed. Cir. 1988)).

Claim 5 is directed to a human monoclonal antibody or functional fragment and a pharmaceutical carrier. Applicant has previously set forth multiple uses sufficient to support the full scope of the claimed invention. For example, the application teaches administration to reduce the proliferation or viability of neoplastic cells (see, for example, page 28, lines 15-17, and page 30, lines 8-12) or to detect neoplastic cells (see, for example, page 28, lines 12-18). The application further provides numerous teachings and guidance for the preparation and use of the claimed human monoclonal antibody for the treatment or diagnosis of a neoplastic condition (see, for example, pages 12-15, and pages 28-34).

Additionally, Applicant has provided extrinsic evidence showing that the use of monoclonal antibodies for the treatment of cancer and other diseases has been well accepted in the art. For example, Applicant has submitted a publication by Walsh, *Nature Biotech.* 18:831-833 (2000), which lists 18 monoclonal antibody-based products that have been approved for medical use in the United States or in the European Union (responses filed February 20, 2001, and December 20, 2002). As described in Walsh and in Applicant's responses, the treatment of cancer with an

antibody-based pharmaceutical composition is a developed art having achieved both commercial and medical success. Accordingly, Applicant has shown that antibody binding to a target antigen is a well recognized means to treat neoplastic diseases

Moreover, the application teaches that the claimed antibody is specific for neoplastic cells and shows relatively little binding to normal cells. For example, the antibody of claim 5 is produced by the hybridoma cell line LH11238. On page 15, lines 19-31, the application teaches:

> The human monoclonal antibodies produced by the hybridoma cell lines LH11238, LH13, H1140, H2420 and H935 all exhibit specific binding to neoplastic cells as compared to normal cells and, therefore, are tumor-specific human monoclonal antibodies. In particular, the human monoclonal antibodies of the invention all selectively bind breast carcinoma cells and show relatively little binding to normal fibroblasts. For example, the LH11238 antibody specifically binds to an antigen present on the surface and lysosomal compartments of breast and ovarian carcinoma cells, as compared to normal fibroblasts, peripheral blood lymphocytes, melanoma cells or lung carcinoma cells.

Id. The above teaching that the claimed antibody is specific to neoplastic cells is further substantiated throughout the application and particularly in Examples I and II.

Example I describes the isolation of the claimed tumor-specific human monoclonal antibody by immuno-screening methods. Example II describes the immunoreactivity of the claimed antibody. In particular, Table 4, page 51, demonstrates that the claimed antibody, produced by hybridoma cell line LH11238, exhibits specific immunoreactivity to breast and ovarian carcinoma. In contrast, no measurable reactivity was observed against normal fibroblasts melanoma or lung carcinoma. Example III confirms the immunoreactivity results determined by ELISA in Example II using flow cytometry (FACS) (see, for example, page 53, line 29 through page 54, line 6, and page 54, lines 18-21). Finally, Examples IV and V demonstrate using immunofluorescence that the neoplastic cell antigen bound by the claimed antibody is present on the cell surface and on lysosomal compartments consistent with membrane internalization (see, for example, page 57, lines 24-27). Accordingly, the application teaches that the claimed antibody exhibits specific binding reactivity to neoplastic cells.

Use of the claimed antibody as a composition with a pharmaceutical carrier, including use in the treatment of a neoplastic condition, would not require undue experimentation. The application teaches sufficient binding specificity of the claimed human monoclonal antibody to allow those skilled in the art to employ it as a binding molecule against neoplastic cells such as breast and ovarian carcinoma cells. Use of an antibody exhibiting binding specificity such as is taught in the application is within the well recognized field of antibody-based compositions amenable to the treatment of diseases. In light of

the well developed state of the art for antibody-based compositions, the teachings and guidance provided in the application with respect to binding specificity of the claimed human monoclonal antibody and the teachings and guidance in the application with respect to use of the claimed human monoclonal antibody to reduce the proliferation or viability of neoplastic cells or to detect neoplastic cells, Applicant contends that the application sufficiently enables those skilled in the art to practice the invention as claimed. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Claim 6 stands newly rejected under 35 U.S.C. §112, first paragraph, as lacking enablement allegedly for a human monoclonal antibody or antigen binding fragment thereof having any conservative substitutions in SEQ ID NOS:2 and 4 that binds any neoplastic cell or antigen thereof.

Applicant contends that the claim is sufficiently enabled because the functional requirement to binding a neoplastic cell or antigen thereof merely ensures that a claimed antibody or functional fragment having a conservative substitution substantially maintains its original binding activity. However, Applicant has amended claim 6 above to recite that an antibody or functional fragment thereof having a conservative substitution of an amino acid binds the same neoplastic cell or antigen thereof as the antibody or functional fragment comprising SEQ ID NOS:2 and 4. Therefore, the amendment clarifies that Applicant's are not claiming conservative substitutions that bind to any neoplastic cell or any neoplastic

antigen. Accordingly, this ground of rejection is rendered moot by the amendment and is respectfully requested to be withdrawn.

CONCLUSION

In light of the Amendments and Remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, he is invited to call the undersigned attorney.

Respectfully submitted,

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